

# Change in Host Behavior and its Impact on the Co-evolution of Dengue

C. P. González\*, K. Herman†, D. Murillo‡, F. Sánchez§

Los Alamos National Laboratory  
Center for Nonlinear Studies  
Los Alamos, NM 87545, U.S.A.

August 8, 2003

## Abstract

The joint evolutionary dynamics of dengue strains are poorly understood despite its high prevalence around the world. Two dengue strains are put in competition in a population where behavioral changes can affect the probability of infection. The destabilizing dynamic effect of even “minor” behavioral changes is discussed and their role in dengue control is explained.

**Keywords:** Vector-transmitted diseases, epidemiology, dengue, behavior change.

## 1 Introduction

Dengue, a mosquito-transmitted disease native to tropical and subtropical climates, was first clinically diagnosed over 200 years ago. However, only recently have scientists begun systematic explorations of dengue, discovering that there are four coexisting strains of the virus around the world. Each strain of dengue is antigenically distinct, meaning that infection caused by one strain of dengue does not confer immunity to infection from another strain. Dengue infection is characterized by the sudden onset of fever, severe headaches, myalgias and arthralgias, leukopenia, thrombocytopenia and on rare occasions infections can lead to the fatal Dengue Haemorrhagic Fever

---

\*Colorado State University-Pueblo

†North Carolina Agricultural and Technical State University

‡Arizona State University

§Cornell University

(DHF). There are between 50 and 100 million cases of dengue reported every year [8]. In this paper we expand upon the work of Esteva and Vargas [9] by including a latent (infected but not infectious) stage for the mosquitoes and the possibility of behavioral change in the host (human) after a first infection (i.e. previous infection with a dengue strain may cause the host to take precautions to avoid further infections). There is a theory that DHF is caused by the interaction of two different strains of dengue. The work in this paper is motivated by a desire to increase the understanding of the mechanisms behind the transmission dynamics of dengue and analyze regions of coexistence of the strains. The article is organized as follows: Section 2 briefly reviews the life-history and ecology of the mosquito as well as the epidemiology of dengue; Section 3 introduces the model for the transmission dynamics of dengue that includes two strains of the virus and a behavior change class; Section 4 includes the computation of the *basic reproductive number*; Section 5 discusses the existence of all equilibria; Section 6 shows the local stability of the disease-free equilibria and necessary conditions for the local stability of the endemic equilibria; Section 7 includes the global stability of the disease-free equilibria; Section 8 introduces the effects of seasonal variations of the mosquito population on dengue infections; Section 9 is a statistical analysis of global dengue data; Section 10 uses parameters estimated from global data to numerically simulate dengue infection; Section 11 combines numerical simulations with seasonal variability; and Section 12 summarizes our results and conclusions of this work.

## 2 Ecology of *Aedes aegypti* and the Epidemiology of Dengue

Dengue, an arbovirus within the family Flaviviridae is transmitted by at least two species of mosquitoes: *Aedes aegypti* (the main vector) and *Aedes albopictus*. These mosquitoes have a four stage life cycle that consists of: egg, larva, pupa and adult stage. We will focus our discussion of the mosquito dynamics on *Aedes aegypti* because they feed mostly on humans while *Aedes albopictus* feed mostly on animals [12]. During the first stage eggs are laid just above the water line in both natural and artificial reservoirs of water. *Ae. aegypti* can lay 150 eggs at once and about 1,400 eggs over her lifetime and these eggs can survive for up to one year in a dry state. Females feed on human blood approximately every 2 to 3 days and may lay eggs after feeding depending on the ambient temperature and environmental factors. After one or two days in favorable conditions, the eggs hatch and the mosquito enters the second stage of its life cycle, the larva. In preparation for the adult stage, seven to ten day old larva undergo metamorphosis in the pupa stage and emerge as an adult after a few days. Male mosquitoes only feed on plants

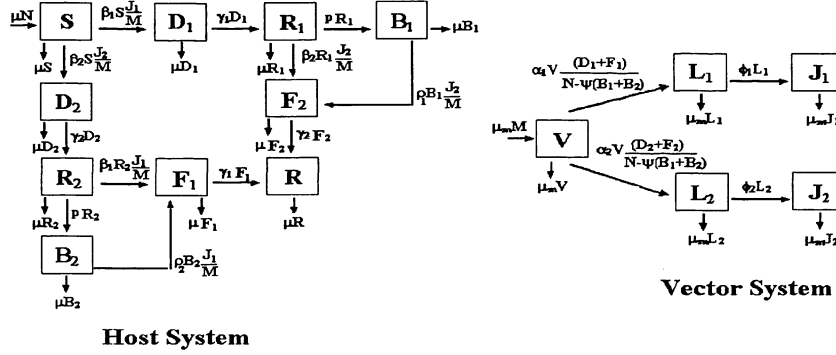


Figure 1: The Model

and flowers. The average duration of the adult stage lasts between 15 to 20 days.

Dengue outbreaks were first reported in Asia, Africa and North America between 1779 – 1780. The exact number of dengue cases is unknown due to the large number of asymptomatic [18] and un-diagnosed infections. Four distinct serotypes coexist (DEN-1, DEN-2, DEN-3, and DEN-4) in various parts of the world [9]. Once infected by a certain serotype, individuals acquire permanent immunity to that serotype, however there is no evidence of cross-immunity (reduced susceptibility to new strains conferred by past infections). The areas at greatest risk of dengue outbreaks are tropical and subtropical regions experiencing high levels of urbanization and increased deforestation [16].

Dengue transmission in humans occurs when an infectious mosquito bites an un-infected human. While there is some evidence of vertical transmission of dengue virus by *Ae. aegypti*, most dengue transmissions in mosquitoes are the result of un-infected mosquitoes biting infected humans. Once the mosquito is infected, the mosquito remains infected for the rest of its life, which is typically 8 to 12 days [12]. The virus produces symptoms that can last up to 14 days in humans. The most deadly form of dengue fever, Dengue Haemorrhagic Fever (DHF), is thought to be caused by the interaction of two or more serotypes [19].

### 3 The Initial Model

Let  $N$  and  $M$  be the host and mosquito populations, respectively. For the hosts, a constant population with birth and death rate  $\mu$  is assumed. Due to the relatively low mortality rate associated with dengue [6], there is no disease induced mortality. The mosquito population is also assumed to be

constant with birth and death rate  $\mu_m$ .

The subscripts  $i, k = 1, 2$  where  $i \neq k$  is used to distinguish between the two strains. The host system is composed as follows:  $S$ , represents susceptible hosts;  $D_i$ , represents hosts initially infected with strain  $i$ ;  $F_i$ , represents hosts with secondary infection of strain  $i$ ;  $B_i$ , represents hosts which change behavior after infection with strain  $i$ ;  $R_i$ , represents hosts which recover from strain  $i$ ;  $R$ , represents hosts that recover from both strains.

$\beta_i$ , represents the transmission rate of strain  $i$  from mosquito to host;  $\gamma_i$  represents the recovery rate of hosts infected with strain  $i$ ,  $p$ , represents the proportion of individuals which change behavior; and  $\rho_k$  represents the transmission rate of strain opposite of  $i$  after changing behavior. Notice that  $\beta_i = \rho_j$  for simplicity in the analysis but also is a reasonable assumption since transmission to a particular strain is approximately equal. In the numerical results we may vary  $\rho_j$ .

The mosquito system is composed as follows: susceptible (adults) mosquitoes,  $V$ ; mosquitoes infected with strain  $i$  but not infectious (latent),  $L_i$ ; mosquitoes infectious with strain  $i$ ,  $J_i$ .  $\alpha_i$ , represents the transmission rate of strain  $i$  from host to mosquito; and  $\phi_i$  represents the rate at which mosquitoes become infective after infection with strain  $i$ . Finally,  $\psi$  represents the effectiveness of the behavior change in the human population. The following nonlinear ODE's are the model equations, represented by the mosquito and host (human) equations, respectively.

$$\begin{aligned}
\frac{dV}{dt} &= \mu_m M - \alpha_1 V \frac{D_1 + F_1}{N - \psi(B_1 + B_2)} - \alpha_2 V \frac{D_2 + F_2}{N - \psi(B_1 + B_2)} - \mu_m V \\
\frac{dL_1}{dt} &= \alpha_1 V \frac{D_1 + F_1}{N - \psi(B_1 + B_2)} - (\mu_m + \phi_1) L_1 \\
\frac{dL_2}{dt} &= \alpha_2 V \frac{D_2 + F_2}{N - \psi(B_1 + B_2)} - (\mu_m + \phi_2) L_2 \\
\frac{dJ_1}{dt} &= \phi_1 L_1 - \mu_m J_1 \\
\frac{dJ_2}{dt} &= \phi_2 L_2 - \mu_m J_2
\end{aligned}$$

where  $M = V + \sum_{i=1}^2 (L_i + J_i)$ .

$$\begin{aligned}
\frac{dS}{dt} &= \mu N - \beta_1 S \frac{J_1}{M} - \beta_2 S \frac{J_2}{M} - \mu S \\
\frac{dD_1}{dt} &= \beta_1 S \frac{J_1}{M} - (\mu + \gamma_1) D_1 \\
\frac{dD_2}{dt} &= \beta_2 S \frac{J_2}{M} - (\mu + \gamma_2) D_2 \\
\frac{dB_1}{dt} &= p R_1 - \rho_1 B_1 \frac{J_2}{M} - \mu B_1 \\
\frac{dB_2}{dt} &= p R_2 - \rho_2 B_2 \frac{J_1}{M} - \mu B_2 \\
\frac{dF_1}{dt} &= \beta_1 R_2 \frac{J_1}{M} + \rho_2 B_2 \frac{J_1}{M} - (\mu + \gamma_1) F_1 \\
\frac{dF_2}{dt} &= \beta_2 R_1 \frac{J_2}{M} + \rho_1 B_1 \frac{J_2}{M} - (\mu + \gamma_2) F_2 \\
\frac{dR_1}{dt} &= \gamma_1 D_1 - \beta_2 R_1 \frac{J_2}{M} - (\mu + p) R_1 \\
\frac{dR_2}{dt} &= \gamma_2 D_2 - \beta_1 R_2 \frac{J_1}{M} - (\mu + p) R_2 \\
\frac{dR}{dt} &= \gamma_1 F_1 + \gamma_2 F_2 - \mu R
\end{aligned}$$

where  $N = S + \sum_{i=1}^2 (D_i + B_i + F_i + R_i + R)$ .

To further simplify the analysis of the system we introduce the following variables to re-scale the model:  $x = \frac{S}{N}$ ,  $y_i = \frac{D_i}{N}$ ,  $u_i = \frac{B_i}{N}$ ,  $z_i = \frac{F_i}{N}$ ,  $v_i = \frac{R_i}{N}$  and  $w = \frac{R}{N}$  (host system). For the mosquito system we have the following:  $a = \frac{V}{M}$ ,  $l_i = \frac{L_i}{M}$  and  $j_i = \frac{J_i}{M}$  where  $i, k = 1, 2$ . Since both the host and mosquito populations are assumed to be constant the system can be reduced

by eliminating the  $R$  equation in the host system and the  $V$  equation in the mosquito system. The following is the re-scaled model:

$$l_i' = \alpha_i \frac{y_i + z_i}{1 - \psi(u_i + u_k)} \left( 1 - \sum_{i=1}^2 l_i - \sum_{i=1}^2 j_i \right) - (\mu_m + \phi_i) l_i \quad (1)$$

$$j_i' = \phi_i l_i - \mu_m j_i \quad (2)$$

where  $a + \sum_{i=1}^2 (l_i + j_i) = 1$ .

$$x' = \mu - \beta_i x j_i - \beta_k x j_k - \mu x, \quad (3)$$

$$y_i' = \beta_i x j_i - (\mu + \gamma_i) y_i, \quad (4)$$

$$u_i' = p v_i - \rho_i u_i j_k - \mu u_i, \quad (5)$$

$$z_i' = \beta_i v_k j_i + \rho_k u_k j_i - (\mu + \gamma_i) z_i, \quad (6)$$

$$v_i' = \gamma_i y_i - \beta_k v_i j_k - (\mu + p) v_i, \quad (7)$$

where  $x + \sum_{i=1}^2 (y_i + u_i + z_i + v_i) + w = 1$

## 4 Basic reproductive number

The *basic reproductive number* represents the number of secondary infections caused by a “typical” infectious individual in a mostly susceptible population when the disease is rare.

Using the next generation operator approach of [3] to calculate  $\mathcal{R}_0$ , the Jacobian of the infectious classes ( $y_i, z_i, j_i$  where  $i = 1, 2$ ) is as follows:

$$\mathcal{A} = \begin{bmatrix} -(\gamma_1 + \mu) & 0 & 0 & 0 & \beta_1 \frac{S}{M} & 0 \\ 0 & -(\gamma_2 + \mu) & 0 & 0 & 0 & \beta_2 \frac{S}{M} \\ 0 & 0 & -(\gamma_1 + \mu) & 0 & \beta_1 \frac{R_2}{M} & 0 \\ 0 & 0 & 0 & -(\gamma_2 + \mu) & 0 & \beta_2 \frac{R_1}{M} \\ \frac{\alpha_1 \phi_1 \frac{V}{N}}{\phi_1 + \mu_m} & 0 & \frac{\alpha_1 \phi_1 \frac{V}{N}}{\phi_1 + \mu_m} & 0 & -\mu_m & 0 \\ 0 & \frac{\alpha_2 \phi_2 \frac{V}{N}}{\phi_2 + \mu_m} & 0 & \frac{\alpha_2 \phi_2 \frac{V}{N}}{\phi_2 + \mu_m} & 0 & -\mu_m \end{bmatrix}. \quad (8)$$

The *basic reproductive number*,  $\mathcal{R}_0$ , for each strain is calculated from the eigenvalues of the matrix  $\mathcal{M} \cdot \mathcal{D}^{-1}$  where  $\mathcal{M}$  and  $\mathcal{D}$  are the decomposition of  $\mathcal{A}$  such that  $\mathcal{D}$  consists of the diagonal elements of  $\mathcal{A}$  where

$$\mathcal{A} = \mathcal{M} - \mathcal{D}$$

with  $\mathcal{M}$  and  $\mathcal{D} > 0$ .

Then the, *basic reproductive number*,  $\mathcal{R}_0$  of the system is defined as:

$$\mathcal{R}_0 = \max\{\mathcal{R}_1, \mathcal{R}_2\} \quad (9)$$

where

$$\mathcal{R}_i = \sqrt{\frac{\alpha_i \phi_i}{\mu_m(\mu_m + \phi_i)} \frac{\beta_i}{(\mu + \gamma_i)}}.$$

In this case the  $\mathcal{R}_0$  can be interpreted as follows: First,  $1/\mu_m$ , is the average lifespan of the mosquito;  $\phi_i/(\mu_m + \phi_i)$ , average time spent in the latent stage by mosquitoes;  $1/(\mu + \gamma_i)$ , average infectious period of the host (human); and  $\alpha_i, \beta_i$  are the transmission rates of mosquito and host respectively.

For simplicity it is assumed that both strains are as likely to infect individuals at risk. Also, note that dengue virus strains are antigenically distinct and therefore one could be more infectious or result in worse illness, but our purpose lies on studying the dynamics of two arbitrary strains and find the regions of existence and co-existence when social dynamics are incorporated.

Next, a local sensitivity analysis is performed on the parameters relevant to the basic reproductive number, that is,  $\phi_i, \alpha_i, \gamma_i, \mu$ , and  $\mu_m$ . And, the parameter with the greatest value is the most sensitive in reducing  $\mathcal{R}_0$  when parameters are varied locally. Next, using [5] we have the following table:

Table 1: Sensitivity Analysis,  $i \in (1, 2)$ .

$\lambda$	$\frac{\lambda}{\mathcal{R}_0} \frac{\partial \mathcal{R}_0}{\partial \lambda}$	Value
$\phi_i$	$\frac{\mu_m}{\mu_m + \phi_i}$	$< 1$
$\alpha_i$	1	$= 1$
$\beta_i$	1	$= 1$
$\gamma_i$	$\frac{\mu}{\mu + \gamma_i}$	$< 1$
$\mu$	$\frac{\gamma_i}{\gamma_i + \mu}$	$< 1$
$\mu_m$	$\frac{2\mu_m + \phi_i}{\mu_m + \phi_i}$	$> 1$

Where the greatest value is obtained by the parameter  $\mu_m$  (Table 1). In biological terms, this implies that by reducing the natural mortality rate of the mosquitoes using insecticide or other control method, the basic reproductive number can be reduced. The questions addressed in this paper are most relevant to social behavior when exposed to multiple infections of dengue fever and possibly the worst case of infection, dengue haemorrhagic fever.

## 5 Existence of disease-free and endemic equilibria

The system has a disease-free equilibrium,  $\xi_0^*$ , when neither strain is present and two nonzero equilibria,  $\xi_1^*$  and  $\xi_2^*$ , where one of the strains is present but not both.

$$\xi_0^* = (1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0), \quad (10)$$

$$\xi_1^* = (x, y_1, 0, 0, 0, v_1, 0, u_1, 0, l_1, 0, j_1, 0), \quad (11)$$

$$\xi_2^* = (x, 0, y_2, 0, 0, 0, v_2, 0, u_2, 0, l_2, 0, j_2). \quad (12)$$

Based on the symmetry of the system we have the following solutions for the solutions for the endemic state.

$$l_i^* = \frac{\mu\mu_m(\mathcal{R}_i - 1)}{\beta_i\phi_i(1 - \delta_i + \nu_i)}, \quad (13)$$

$$j_i^* = \frac{\mu(\mathcal{R}_i - 1)}{\beta_i(1 - \delta_i + \nu_i)}. \quad (14)$$

$$x^* = \frac{\nu_i + 1 - \delta_i}{\nu_i + \mathcal{R}_i - \delta_i}, \quad (15)$$

$$y_i^* = \frac{\mu(\mathcal{R}_i - 1)}{(\mu + \gamma_i)(\mathcal{R}_i - \delta_i + \nu_i)}, \quad (16)$$

$$u_i^* = \frac{\delta_i(\mathcal{R}_i - 1)}{\psi(\mathcal{R}_i - \delta_i + \nu_i)}, \quad (17)$$

$$v_i^* = \frac{\mu\gamma_i(\mathcal{R}_i - 1)}{(\mu + \gamma_i)(\mu + p)(\mathcal{R}_i - \delta_i + \nu_i)}, \quad (18)$$

Where

$$\delta_i = \frac{p\psi\gamma_i}{(\mu + p)(\mu + \gamma_i)},$$

and

$$\nu_i = \frac{\alpha_i}{\mu_m} \frac{\mu}{\mu + \gamma_i}.$$

Two quantities show up frequently in the analysis of our equilibria and have the following biological meaning:  $\delta_i$ , represents the risk of being infected with a second strain after changing behavior and  $\nu_i$  represents the efficacy of human transmission of dengue to mosquitoes. For  $\delta_i$ ,  $\psi$  is the effectiveness of behavior change,  $p$  is the proportion of individuals that change behavior,  $\gamma_i$  is the recovery rate from strain  $i$ ,  $\gamma_i/(\mu + \gamma_i)$  is the proportion of individuals that survive from infection to the recovered class; and  $p/(\mu + p)$  is the proportion



of individuals that survive to the behavior change class,  $u_i$  from the recovered class. For  $\nu_i$ ,  $\mu/(\mu + \gamma_i)$  is the proportion of humans that die in the infected class,  $\alpha_i$  is the transmission rate of infection from humans to mosquitoes, and  $1/\mu_m$  is the average life span of mosquitoes.

**Lemma 5.1.** *It is a necessary condition for the existence of the endemic equilibria that  $\mathcal{R}_0 > 1$  and  $\delta_i < 1$ , for  $i = 1, 2$ .*

*Proof.* From equation  $j_i^*$  it is clear that  $\mathcal{R}_0$  must be greater than one in order for the equilibria to exist. We are left to evaluate the inequality  $\delta_i < 1$ , which is equivalent to

$$p\gamma_i\psi < (\text{pos.terms}) + \gamma_ip.$$

where  $\psi \in [0, 1)$ . Hence, the inequality holds. This result also implies the fact that when  $p = 0$ ,  $\psi$  no longer affects the dynamics.  $\square$

## 6 Local stability of disease-free equilibria and necessary conditions for the stability of endemic equilibria

Next, the local stability of the disease-free equilibrium is determined.

**Theorem 6.1.** *Let  $\vec{\xi}_0^* = (1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0)$  be a positive disease-free equilibrium of (1) - (7) then the disease-free equilibrium is locally asymptotically stable if and only if  $\mathcal{R}_0 < 1$ .*

*Proof.* The analysis results in the eigenvalues of the Jacobian<sup>2</sup> matrix evaluated at the the disease-free equilibrium where,  $-1$  ( of multiplicity two ),  $-\mu$  ( of multiplicity three ),  $-(\mu + \gamma_1)$ , and  $-(\mu + \gamma_2)$ . It remains only to verify that all the zeros of the cubic factors of (19)-(20) contain negative real parts.

$$\lambda^3 + (2\mu_m + \gamma_1 + \phi_1 + \mu)\lambda^2 + (\mu_m(\mu_m + \phi_1) + (\mu + \gamma_1)(2\mu_m + \phi_1))\lambda + \mu_m(\mu_m + \phi_1)(\mu + \gamma_1)(1 - \mathcal{R}_1) = 0, \quad (19)$$

and,

$$\lambda^3 + (2\mu_m + \gamma_2 + \phi_2 + \mu)\lambda^2 + (\mu_m(\mu_m + \phi_2) + (\mu + \gamma_2)(2\mu_m + \phi_2))\lambda + \mu_m(\mu_m + \phi_2)(\mu + \gamma_2)(1 - \mathcal{R}_2) = 0. \quad (20)$$

---

<sup>2</sup>See Appendix

From the Routh-Hurwitz criteria we have  $a_1 > 0$  and  $a_3 > 0$  if  $\mathcal{R}_0 < 1$  since all parameters are nonnegative. Therefore, we are left to verify the condition  $a_1 a_2 - a_3 > 0$ .

Thus,

$$(2\mu_m + \gamma_i + \phi_i + \mu)(\mu_m(\mu_m + \phi_i) + (\mu + \gamma_i)(2\mu_m + \phi_i)) > \mu_m(\mu_m + \phi_i)(\mu + \gamma_i)(1 - \mathcal{R}_0), \quad (21)$$

and,

$$2\mu_m(2\mu_m + \phi_i)(\mu + \gamma_i) + (pos.terms) > \mu_m(\mu_m + \phi_i)(\mu + \gamma_i). \quad (22)$$

where  $i = 1, 2$ . Hence, the Routh-Hurwitz criteria holds.  $\square$

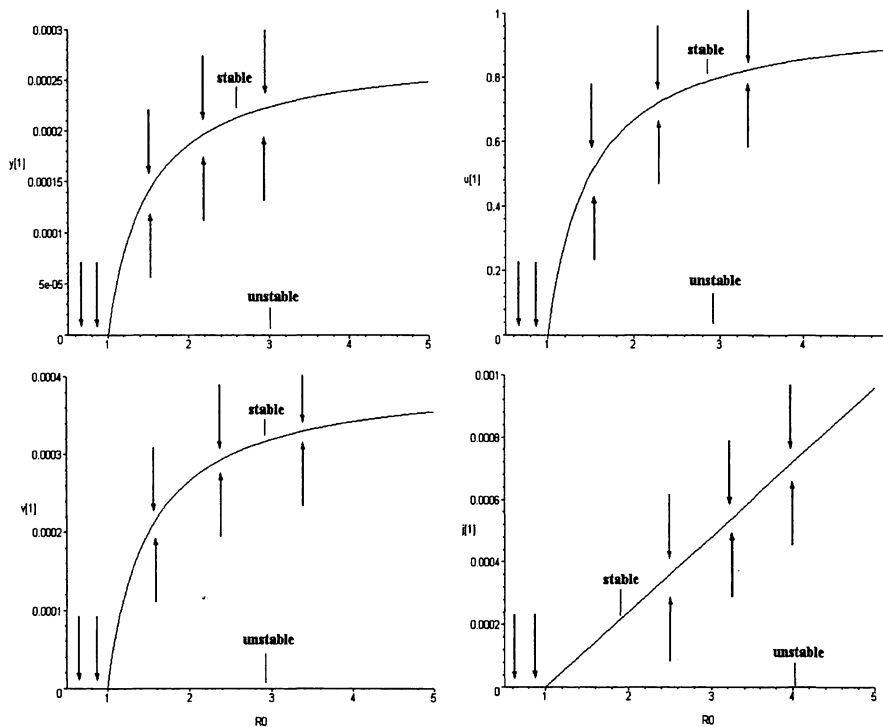


Figure 2: Forward bifurcations in terms of  $\mathcal{R}_0$ .

In Figure 2 we have the forward bifurcations in terms of  $\mathcal{R}_0$  and  $y_1$ ,  $u_1$ ,  $v_1$  and  $j_1$ . Clearly, when  $\mathcal{R}_0 < 1$  the disease-free is stable and unstable otherwise.

**Proposition 6.2.** *It is a necessary condition for the local asymptotic stability of the endemic equilibria that (for  $i, k = 1, 2, i \neq k$ )*

$$\mathcal{R}_i^2 < \left[ \frac{1 - (\mathcal{R}_k^2 - 1) \frac{\delta_k}{(\nu_k + \mathcal{R}_k^2 - \delta_k)}}{1 - (\mathcal{R}_k^2 - 1) \mu \frac{\mu_m + \phi_k}{\beta_k \phi_k (\nu_k + 1 - \delta_k)}} \right] \left[ \frac{(\nu_k + \mathcal{R}_k^2 - \delta_k)}{\frac{\gamma_k (\mathcal{R}_k^2 - 1)}{(\mu + \gamma_k)} + (\nu_k + 1 - \delta_k)} \right] \quad (23)$$

*Proof.* We show that all the eigenvalues of the sub-matrix  $G2^3$  have negative real part. The problem easily reduces to determining the eigenvalues of the real part of the cubic factor of the characteristic polynomial,

$$p(\lambda) = \lambda^3 + (2\mu_m + \mu + \gamma_1 + \phi_1)\lambda^2 + [(\mu_m + \phi_1)(\mu + \gamma_1) + \mu_m(\mu + \gamma_1 + \mu_m + \phi_1)]\lambda + \left[ \mu_m(\mu_m + \phi_1)(\mu + \gamma_1) - h_5(h_6\phi_1 + \frac{\beta_1\phi_1(\nu_2 + 1 - \delta_2)}{\nu_2 + \mathcal{R}_2 - \delta_2}) \right], \quad (24)$$

of this sub-matrix.

With  $a_1$ ,  $a_2$ , and  $a_3$  the quadratic, linear, and constant coefficients, respectively. It is easy to see that  $a_1, a_2$  are positive, and that terms cancel sufficiently to prove  $a_1 a_2 - a_3 > 0$ . The inequality of the proposition is, after substitution of the expressions of  $h_5$  and  $h_6$ , the condition that  $a_3 > 0$ . Thus, the inequality (23) insures that the Routh-Hurwitz criteria are satisfied and hence all eigenvalues have negative real part.  $\square$

In Figure 3 there are four regions of stability for various parameter values. All parameters are taken from Table 2 except where noted. “DF” represents the disease free equilibrium that is stable when  $\mathcal{R}_0 < 1$ . Region *I* represents local stability of the endemic equilibrium for strain 1 when  $\mathcal{R}_1 > 1$  and region *II* represents the analogous case for  $\mathcal{R}_2 > 1$ . Region *III* represents the co-existence of both strains. Different parameter values can greatly affect the size of region *III*, but not the overall dynamics of the stability regions.

## 7 Global stability of disease-free equilibria

Next, the global stability of the disease-free equilibria is determined.

**Theorem 7.1.** *Assume  $\beta_i = \rho_k$ , for  $i \neq k$ ,  $\psi = 0$  and  $\mathcal{R}_0 < 1$ , then the positive disease-free equilibrium given by (10) is globally asymptotically stable on the domain  $\Omega = \{(x, y_i, u_i, z_i, v_i, w, a, l_i, j_i) | x + \sum_{i=1}^2 (y_i + u_i + z_i + v_i) + w = 1, a + \sum_{i=1}^2 l_i + \sum_{i=1}^2 j_i = 1\} \subset \mathbb{R}_+^{15}$  for  $i = 1, 2$ .*

---

<sup>3</sup>See Appendix for terms  $h_5$  and  $h_6$

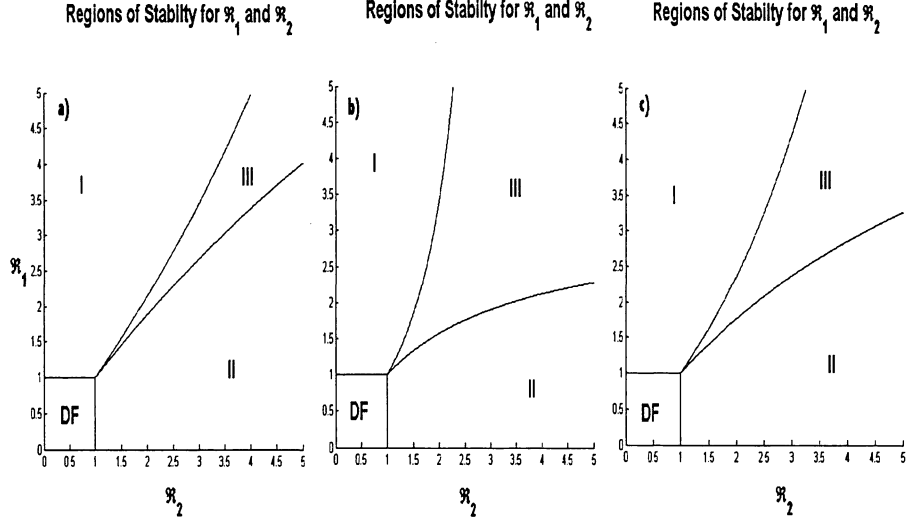


Figure 3: Regions of stability when a)  $\alpha_1 = \beta_1 = 0.2, \alpha_2 = \beta_2 = 0.2, \gamma_1 = 0.33, \psi = 0.5, p = 0.1$  and b)  $\alpha_1 = \alpha_2 = 0.2, \beta_1 = \beta_2 = 0.5, \gamma_2 = 0.33, \psi = 0.9, p = 0.9$  and c)  $\alpha_1 = \beta_1 = 0.2, \alpha_2 = \beta_2 = 0.5, \gamma_1 = 0.33, \psi = 0.5, p = 1$ .

*Proof.* We construct the following Lyapunov function, where  $i, k = 1, 2$  and  $i \neq k$ .

$$\mathcal{L} = \sum_{i=1}^2 \left( \frac{\beta_i}{\mu_m(\mu_m + \phi_i)} j_i + l_i + y_i + z_i \right) \geq 0,$$

where the orbital derivative is given by

$$\dot{\mathcal{L}} = \sum_{i=1}^2 \left( -(\mu + \gamma_i)(y_i + z_i) \left[ 1 - \mathcal{R}_0 \left( 1 - \sum_{i=1}^2 l_i - \sum_{i=1}^2 j_i \right) \right] - \phi_i l_i \left( \frac{\beta_i}{\mu_m} - 1 \right) + \beta_i j_i (1 - (y_k + z_k)) \right) \leq 0$$

By inspection and with  $\beta_i$  sufficiently small but greater than  $\mu_m$ ,  $\dot{\mathcal{L}} \leq 0$ .  $\square$

## 8 Seasonal Variation Model

We now examine a seasonal variation model that uses a recruitment function, which takes into account the seasonality of the mosquito population in some tropical regions. There is evidence that suggests the mosquito population is related to the number and location of breeding sites in a region [12]. Thus, during the rainy seasons there is an increase in breeding sites, which results in

an increase in the population density of mosquitoes. This introduces seasonal variation to the mosquito population.

To incorporate an approximation for the seasonal variation in the model, we choose a recruitment function that is periodic in time. Specifically, we choose a cosine function so that the rainy season corresponds to the peak of our function and the off-peak season corresponds to the minimum of our function:

$$\eta_0 + \eta_1 \cos(\omega t + \phi).$$

We choose  $\eta_0$  to be the average recruitment rate such that our recruitment is always positive. We choose  $\eta_1$  such that our function is strictly positive.  $\omega$  is chosen such that it is  $1/T$  where  $T$  represents the period of the seasonal variation (one year),  $t$  is unit time and  $\phi$  is the phase shift.

The host system remains invariant while the mosquito system has a change in the susceptible class as follows:

$$\begin{aligned} \frac{dV}{dt} = & \mu_m M(\eta_0 + \eta_1 \cos(\omega t + \phi)) - \alpha_1 V \frac{D_1 + F_1}{N - \psi(B_1 + B_2)} \\ & - \alpha_2 V \frac{D_2 + F_2}{N - \psi(B_1 + B_2)} - \mu_m V. \end{aligned} \quad (25)$$

Note that now the mosquito system has a non-constant population. Therefore we add a new equation to the mosquito system:

$$\frac{dM}{dt} = \mu_m M(\eta_0 + \eta_1 \cos(\omega t + \phi)) - 1). \quad (26)$$

## 9 World dengue data

There has been growing interest concerning the prevalence of dengue in the world. In particular, the World Health Organization is making the attempt to increase the awareness of this disease by increasing the reported cases of dengue [20]. The number of dengue cases reported each year varies dramatically and has reached a peak in 1998 (see Figure 4), followed by a sharp decrease and a steadily increasing number of cases in the past few years.

While dengue cases vary widely per year, there are also strong seasonal variations within a year. This phenomenon is most prevalent in tropical and sub-tropical climates like Puerto Rico as illustrated in Figure 6. In particular, there is a sharp decrease in dengue cases in February due to the start of the dry season.

We can normalize the number of dengue cases by the mean value for that particular year and see that they each follow the same pattern: a marked

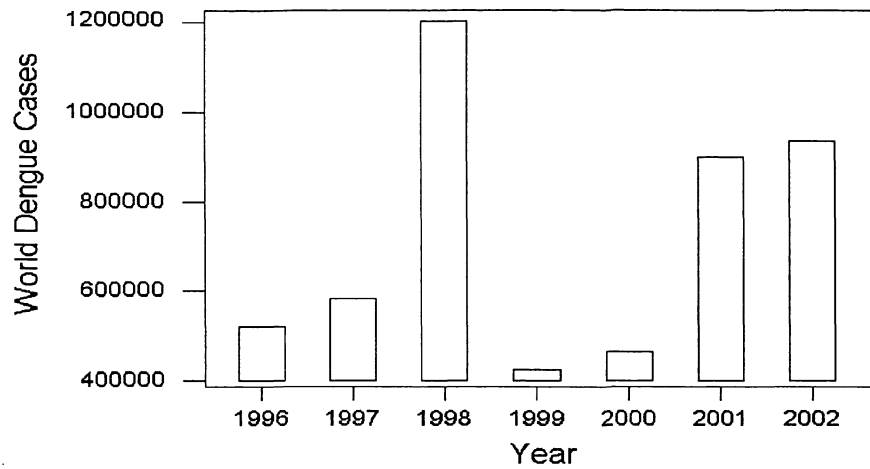


Figure 4: Large variations in World Dengue Cases.

drop in February followed by near constant numbers of cases (see Figure 6). Analyzing the percent variation makes this pattern very clear. In fact, February cases are generally over two and a half standard deviations below the mean, with a p-value  $\approx 0.0001$  for the mean. This is a strong indicator that the seasonality displayed is not due to random noise and can be predicted (see Figure 7).

Another interesting aspect of our data comes in the ratio of cases per incidence. The ratio is nearly constant at 33.48 indicating that the parameter values of infectious force are nearly constant. This result supports the model and allows us to consider all parameters of infectious force as constants and independent of time.

## World Distribution of Dengue - 2000

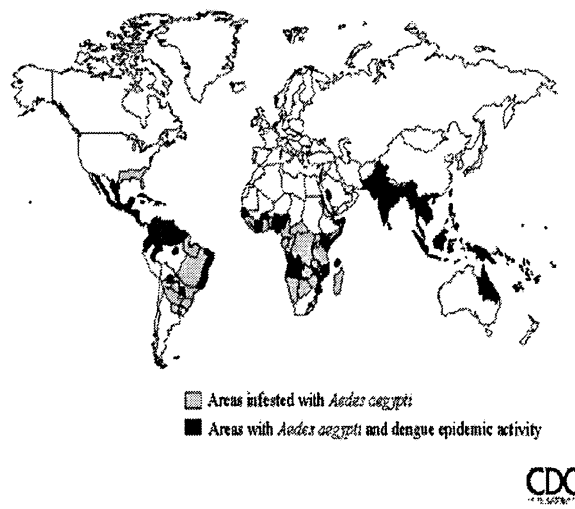


Figure 5: World Distribution of Dengue, 2000.

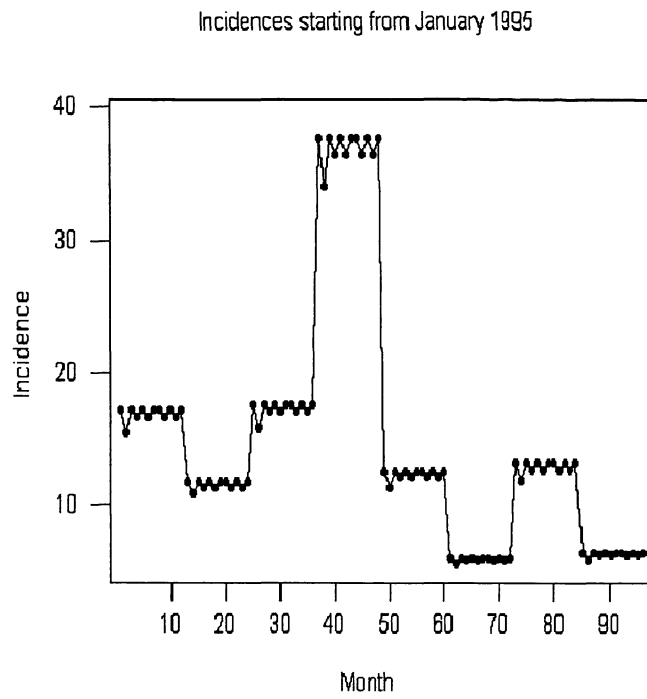


Figure 6: Incidence of Dengue in Puerto Rico.

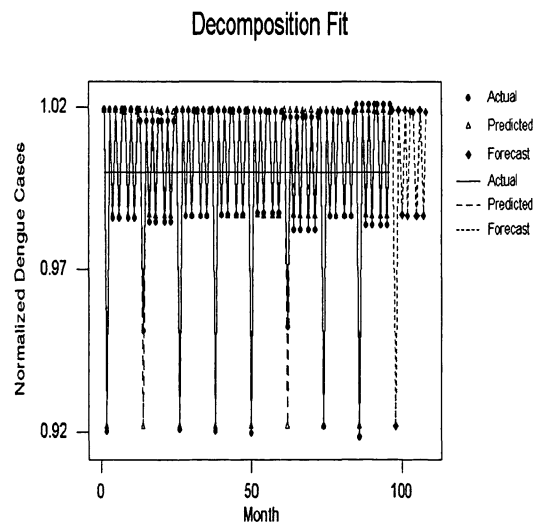


Figure 7: Periodic behavior of dengue in tropical areas.



## 10 Numerical Simulations

For the simulations, the parameters  $\alpha_i$ ,  $\beta_i$ ,  $\rho_k$ ,  $p$ , and  $\psi$  were varied while maintaining  $\mu$ ,  $\mu_m$ ,  $\phi_i$ , and  $\gamma_i$  constant. Parameter values and initial conditions are chosen to be biologically accurate as to display the behavior of our model. The parameters  $\mu$ , and  $\mu_m$  were determined from dengue outbreak studies [10, 9]. For the rest of the section the values in Table 2 are used, unless otherwise noted for the specific simulation being discussed:

Table 2: Parameter values and initial conditions

Parameter	Value	State Variable	Initial Value
$\alpha_i$	0.5	$a$	0.9
$\beta_i$	0.5	$l_i$	0
$\gamma_i$	0.14	$j_i$	0.05
$\mu_m$	0.033	$x$	0.9
$\mu$	0.00004	$y_i$	0.05
$\phi_i$	0.1	$z_i$	0
$\rho_i$	0.2	$u_i$	0
$\psi$	0.5	$v_i$	0
$p$	0.1	$w$	0

In Figure 8 the system is considered when zero percent of the population leaving the recovery class and entering the behavior class changes its behavior after a primary infection, that is  $p = 0$ . Note when  $p = 0$ ,  $\psi$  no longer affects the transmission dynamics of the system. The transmission dynamics of dengue continues to affect both mosquito and host populations without any intervening measures, such as implementing dengue control measures. Excluding the behavioral class, which remains at zero for all time, the mosquito and host systems display dampened oscillatory behavior. Damped oscillations display the transmission dynamics of dengue which appears in a population, disappears gradually, and then reappears in the population to eventually reach an equilibrium.

Next in Figure 9, we consider the system when  $p = 1$  and  $\psi = 1$ . These are ideal conditions for effective control strategies initiated by a region infected with dengue serotypes since most of the population is taking some precautions and they are very effective. If these conditions are attained after dengue has been introduced into a population, the number and frequencies of oscillations will be decreased in both host and mosquito populations. Incorporating the behavioral change class in the dynamics of this system will result in greater damped oscillations in the infected host and mosquito pop-

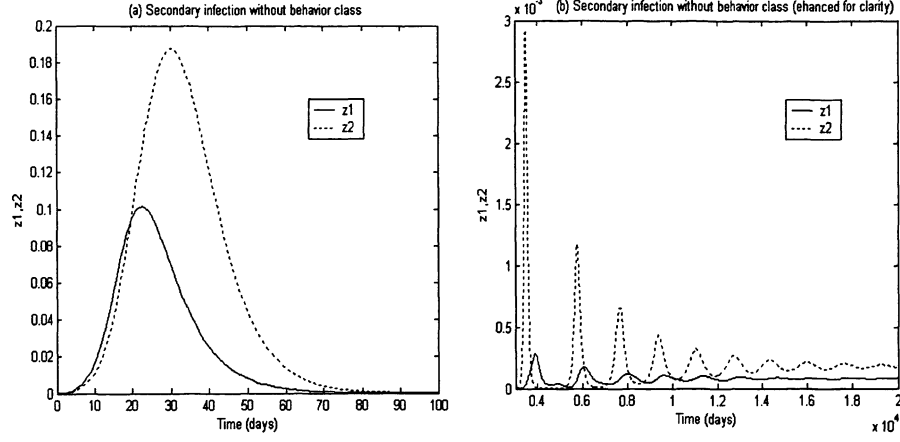


Figure 8: (a) The secondary infection classes,  $z_1$  and  $z_2$  (b) The secondary infection classes,  $z_1$  and  $z_2$ , enhanced for clarity when  $p = 0$  and  $\psi = 0$ .

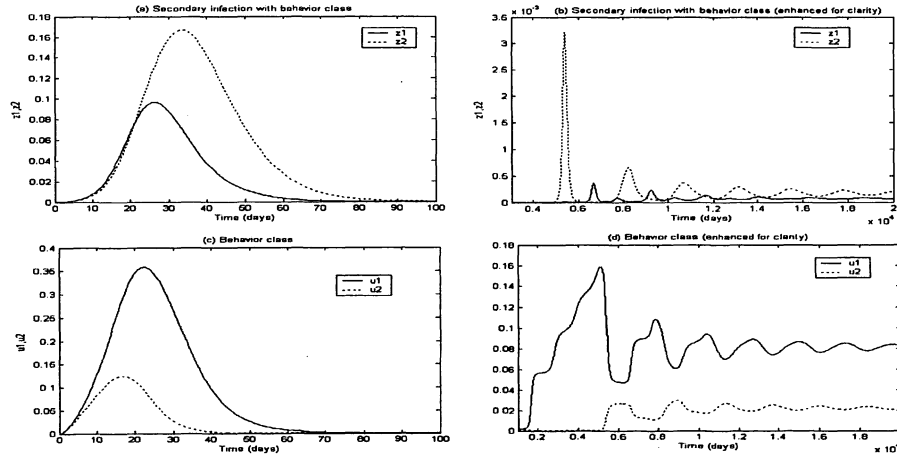


Figure 9: (a) The secondary infection classes,  $z_1$  and  $z_2$  (b) The secondary infection classes,  $z_1$  and  $z_2$ , enhanced for clarity when  $p = 1$  and  $\psi = 1$ .

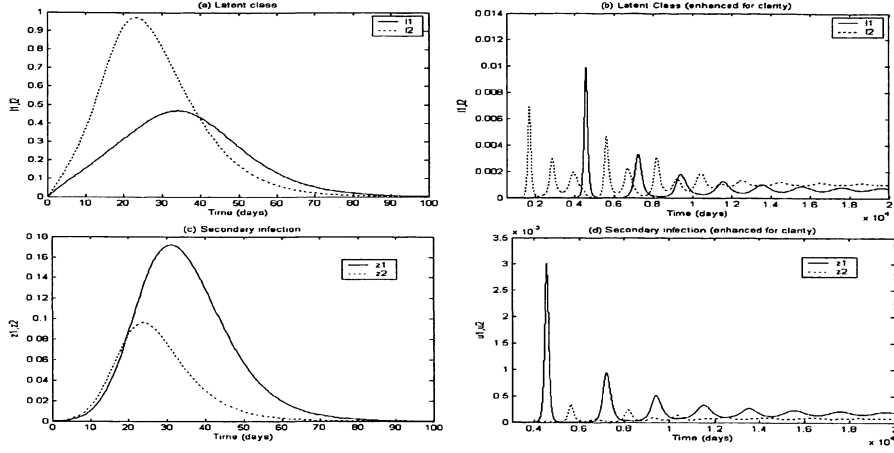


Figure 10: (a) The secondary infection classes  $z_1$  and  $z_2$  (b) The secondary infection classes  $z_1$  and  $z_2$  enhanced for clarity (c) The latent classes  $l_1$  and  $l_2$  (d) The latent classes  $l_1$  and  $l_2$  enhanced for clarity, when  $p = 0.1$ ,  $\psi = 0.5$ ,  $\alpha_1 = 1/3$ ,  $\beta_1 = 1/3$ ,  $\alpha_2 = 1/2$ , and  $\beta_2 = 1/2$ .

ulations. The damped oscillatory trend of the behavioral class represents the host population's response to the oscillatory nature of dengue transmission. A decrease in behavioral change practices results in the sudden reappearance of dengue in a population; subsequently, the population increases its behavioral change practices.

In Figure 10, the system is analyzed with 10% of the population leaving the recovery classes to enter the behavior change classes and the effectiveness of their behavior change is 50%, that is  $p = 0.1$  and  $\psi = 0.5$ . Strain 2 is the dominant strain in the population with  $\alpha_1 < \alpha_2$  and  $\beta_1 < \beta_2$  (i.e.  $\alpha_1 = 1/3$  and  $\beta_1 = 1/3$ ). This conclusion can be easily seen for Figure 12, (a) and (b), the latent stage of the mosquito system, where the largest peak corresponds to the dominant strain present in the population. However, (c) and (d), the secondary infection classes, must be analyzed from a different perspective. Due to the large amount of susceptible host population entering the primary infection class of strain 2, these individuals will be taking precautionary measures for the prevention of becoming infected with strain 1; this results in a larger population entering the secondary infection class of strain 1. The same will also be true for the behavior class of strain 1.

In Figure 11, the system is also considered when  $p = 0.1$ , but the effectiveness of there behavior change is 0, i.e.  $\psi = 0$ . The transmission rates of infection are unequal, that is  $\alpha_1 = 1/3$ ,  $\beta_1 = 1/3$ ,  $\alpha_2 = 1/2$ ,  $\beta_2 = 1/2$ , and  $\rho_i = 1/5$ . In this case, a portion of the population leaving the recover classes and entering the behavior classes is implementing dengue control methods,

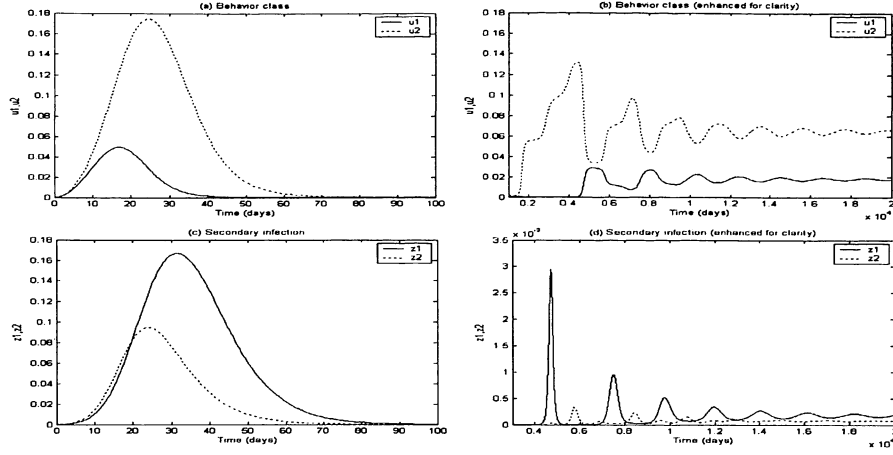


Figure 11: (a) The behavior classes  $u_1$  and  $u_2$  (b) The behavior classes  $u_1$  and  $u_2$  enhanced for clarity (c) The secondary infection classes  $z_1$  and  $z_2$  (d) The secondary infection classes  $z_1$   $z_2$  enhanced for clarity, when  $p=0.1$ ,  $\psi = 0$ ,  $\alpha_1 = 1/3$ ,  $\beta_1 = 1/3$ ,  $\alpha_2 = 1/2$ , and  $\beta_2 = 1/2$ .

but their preventive measures are not effective in decreasing the spread of infection. Strain 2 is the dominant strain in the population. Due to the large amount of the population entering the primary infection class of strain 2, these individuals will be changing their behavior in the prevention of becoming infected with strain 1; this results in a larger population of the previously specified population entering the behavior class and secondary infection classes of strain 1.

Finally in Figure 12, the system was simulated with parameter values that will result in  $\mathcal{R}_2 < 1$ , that is the population will be rid of dengue infection. For  $\mathcal{R}_2 < 1$ , we let  $\alpha_2 = 1/15$  and  $\beta_2 = 1/15$ . Thus, strain 2 vanishes as time increases and will not reappear in the population.

## 11 Simulations with Seasonality

The introduction of seasonality requires 4 control parameters:  $\eta_0$  which controls the growth of the mosquito population,  $\eta_1$  which controls the strength of the seasonality,  $\omega$  which controls the frequency of oscillation and  $\phi$  which controls the phase of oscillations. The control parameters play a large role in determining the dynamics of the system.  $\eta_0$  dictates whether the population will eventually die out, go unbounded, or reach a steady mean value. Oscillations in both mosquito and host classes can be induced by  $\eta_1$  and  $\omega$  can determine the nature of the oscillations while  $\phi$  is the phase shift. The most important feature, however, is that the seasonality term is an explicit

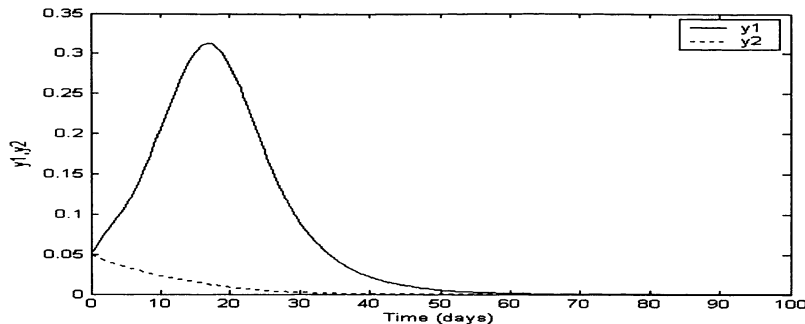


Figure 12:  $y_1$  when  $\mathcal{R}_1 > 1$  and  $y_2$  when  $\mathcal{R}_2 < 1$ .

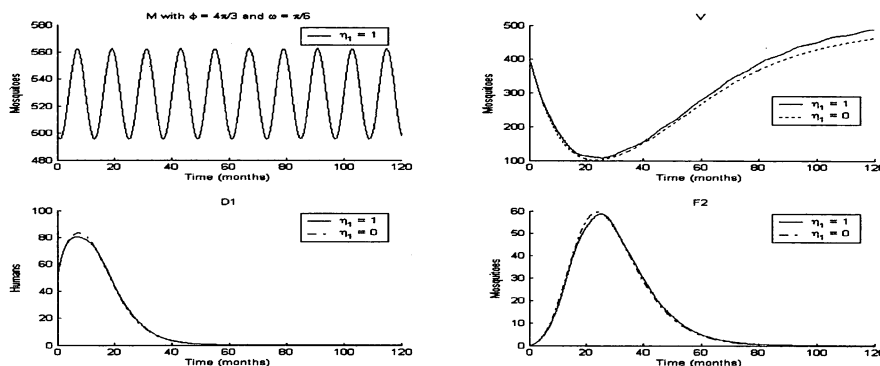


Figure 13:  $y_1$  when  $\mathcal{R}_1 > 1$  and  $y_2$  when  $\mathcal{R}_2 < 1$ .

function of time. That is, the system of equations is now non-autonomous. This adds a great deal of complexity to the analysis and numerical solutions were sought in order to address this issue. Figure 13 is a summary of our results. We see that adding the seasonality term has a tremendous impact on the total mosquito population. It was previously assumed that the mosquito population was constant and that allowed for the re-scaling of the system of equations, transforming them into a very tractable form. Figure 13 (a) clearly shows that the total mosquito population is not constant and in fact is periodic in time. In Figure 13 (b) we see that while these periodic oscillations are also evident in the number of susceptible mosquitoes, the dynamics of that class are dominated by the initial growth and decay terms. The oscillations are of very low amplitude and do not effect the overall dynamics significantly. Looking at Figure 13 (c) and (d), there is little change between the system with seasonality and without.

## 12 Conclusions

A model for the transmission dynamics of two strains of dengue, a mosquito-transmitted disease, was formulated and analyzed with the incorporation of a behavioral change class. In a region where two serotypes of dengue are present, the incorporation of a behavioral change class may be essential to more accurately model host and mosquito populations in efforts to implement disease control methods. After a primary infection and the severe medical complications that may accompany the infection, a once primary infected susceptible individual may change his or her behavior to prevent a possible secondary infection. The model shows that the rate of secondary infections is influenced greatly through the incorporation of a behavioral change class. As to further incorporate factors that may influence the transmission dynamics of dengue, we formulated and analyzed a model incorporating seasonal variations in the mosquito population. Dengue outbreaks may occur during dry seasons and periods of non-elevated mosquito populations, this second model shows elevated populations of mosquitoes associated with rainy conditions insufficiently affect the transmission rate of infection in both host and mosquito systems [12].

In the initial model, the local and global stability of the disease free equilibria and the existence of two possible endemic equilibria were established. Incorporating the behavioral change class,  $\delta_i$ , the risk of being infected with a second strain after changing behavior, is an important limitation for the existence of endemic equilibria, as well as  $\mathcal{R}_0$ .

When we add seasonal variation to our initial model, we get oscillations in the total mosquito population, but the overall dynamics remain unchanged.

The two framework presented attempt to more accurately model two factors that may affect dengue transmission dynamics, host population behavioral change and seasonal variations of the mosquito population. Our results support the necessity of a behavioral change class to model the transmission dynamics of dengue. A behavioral change constitutes any control methods implemented by a once primarily infected, susceptible population. Any proportion of that population implementing control methods results in a dramatic decrease of the infectious and infected mosquito population rates as shown in section 8 outlining numerical simulations. Control methods instituted by those individuals may be an effective method to control dengue outbreaks. Heighten control methods implemented continuously may also be an effective method to lessen the rate of dengue outbreaks.

Social behavior plays a major role in the evolution of infectious diseases. There are tremendous challenges in modeling social dynamics. Provided the implementation of better measures is not effectively communicated to the public, and therefore progress is not being made. We are our best allies in fighting diseases, but innovating methods must be presented in order to have

a bigger impact on future generations.

## 13 Acknowledgements

We would like to thank Carlos Castillo-Chávez for all of his valuable advice and guidance. We would also like to thank Song Baojun, Martin Engman and Juan Pablo Aparicio for providing us with helpful mathematical material. Also, we would like to thank Terannie Vázquez for lending us her computer for the entire eight weeks to work on our project.

This research has been partially supported by grants given by the National Science Foundation, National Security Agency, and the Sloan Foundation (through Cornell-Sloan National Pipeline Program in the mathematical Sciences). Substantial financial and moral support was also provided by the T Division of Los Alamos National Lab (LANL), CNLS at LANL, Office of the Provost of Cornell University, and the Dept. of Biological Statistics & Computational Biology. The authors are solely responsible for the views and opinions expressed in this research; it does not necessarily reflect the ideas and/or opinions of the funding agencies, Cornell University, and/or LANL.

## 14 Appendix

The Jacobian of the system (1) - (7) is given by,

$$J(\vec{\xi}) = \begin{bmatrix} J_1 & J_2 \\ J_3 & J_4 \end{bmatrix}$$

where,

$$J_1 = \begin{bmatrix} \frac{f_1}{1-(u_1+u_2)} & -\frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} \\ \frac{f_1}{1-(u_1+u_2)} & -\frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} \\ \frac{f_1}{1-(u_1+u_2)} & -\frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} \\ \frac{f_1}{1-(u_1+u_2)} & -\frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} \\ \frac{f_1}{1-(u_1+u_2)} & -\frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} \\ \frac{f_1}{1-(u_1+u_2)} & -\frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} \\ \frac{f_1}{1-(u_1+u_2)} & -\frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} \\ \frac{f_1}{1-(u_1+u_2)} & -\frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} & \frac{f_1}{1-(u_1+u_2)} \end{bmatrix}$$

$$J_2 = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \frac{\alpha_2(1-l_1-l_2-j_1-j_2)(y_2+z_2)\psi}{(1-\psi(u_1+u_2))^2} & -\frac{\alpha_2(y_2+z_2)}{1-\psi(u_1+u_2)} & -\frac{\alpha_2(y_2+z_2)}{1-\psi(u_1+u_2)} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$J_3 = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \frac{\alpha_1(1-l_1-l_2-j_1-j_2)(y_2+z_2)\psi}{(1-\psi(u_1+u_2))^2} & -\frac{\alpha_1(y_1+z_1)}{1-\psi(u_1+u_2)} & -\frac{\alpha_1(y_1+z_1)}{1-\psi(u_1+u_2)} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \beta_1 j_1 & \rho_2 j_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\beta_2 x & 0 & 0 & 0 & 0 \end{bmatrix}$$





The following values are found in  $J(\vec{\xi}^*(EE))$ ,

$$\begin{aligned}
h_1 &= \frac{\alpha_2 \left(1 - \frac{\mu_m \mu (\mathcal{R}_2 - 1)}{\beta_2 \phi_2 (\nu_2 + 1 - \delta_2)} - \frac{\mu (\mathcal{R}_2 - 1)}{\beta_2 (\nu_2 + 1 - \delta_2)}\right)}{1 - \frac{\delta_2 (\mathcal{R}_2 - 1)}{\nu_2 + \mathcal{R}_2 - \delta_2}} \\
h_2 &= \frac{\alpha_2 \mu \psi (\mathcal{R}_2 - 1) \left(1 - \frac{\mu_m \mu (\mathcal{R}_2 - 1)}{\beta_2 \phi_2 (\nu_2 + 1 - \delta_2)} - \frac{\mu (\mathcal{R}_2 - 1)}{\beta_2 (\nu_2 + 1 - \delta_2)}\right)}{(\mu + \gamma_2) (\nu_2 + \mathcal{R}_2 - \delta_2) \left(1 - \frac{\delta_2 (\mathcal{R}_2 - 1)}{\nu_2 + \mathcal{R}_2 - \delta_2}\right)^2} \\
h_3 &= -\frac{\alpha_2 \mu (\mathcal{R}_2 - 1)}{(\mu + \gamma_2) (\nu_2 + \mathcal{R}_2 - \delta_2) \left(1 - \frac{\delta_2 (\mathcal{R}_2 - 1)}{\nu_2 + \mathcal{R}_2 - \delta_2}\right)} - (\phi_2 + \mu_m) \\
h_4 &= -\frac{\alpha_2 \mu (\mathcal{R}_2 - 1)}{(\mu + \gamma_2) (\nu_2 + \mathcal{R}_2 - \delta_2) \left(1 - \frac{\delta_2 (\mathcal{R}_2 - 1)}{\nu_2 + \mathcal{R}_2 - \delta_2}\right)} \\
h_5 &= \frac{\beta_1 \mu \delta_2 (\mathcal{R}_2 - 1)}{p \psi (\nu_2 + \mathcal{R}_2 - \delta_2)} + \frac{\rho_2 \delta_2 (\mathcal{R}_2 - 1)}{\psi (\nu_2 + \mathcal{R}_2 - \delta_2)} \\
h_6 &= \frac{\alpha_1 \left(1 - \frac{\mu_m \mu (\mathcal{R}_2 - 1)}{\beta_2 \phi_2 (\nu_2 + 1 - \delta_2)} - \frac{\mu (\mathcal{R}_2 - 1)}{\beta_2 (\nu_2 + 1 - \delta_2)}\right)}{1 - \frac{\delta_2 (\mathcal{R}_2 - 1)}{\nu_2 + \mathcal{R}_2 - \delta_2}}
\end{aligned}$$

## References

- [1] Brauer, F., Castillo-Chávez, C., *Mathematical Models in Population Biology and Epidemiology*, Texts in Applied Mathematics, **40**, Springer-Verlag, New York 2001.
- [2] Busenberg, S., Cooke, K., *Vertically Transmitted Diseases*, Biomathematics, **23**, Springer-Verlag, 1993.
- [3] Castillo-Chávez, C., Z. Feng, W. Huang, *On the Computation of  $\mathcal{R}_0$  and its Role on Global Stability* in Mathematical Approaches for emerging and re-emerging infectious diseases, Part I, IMA, **125**, Springer-Verlag, New York, pp. 224-250.
- [4] Castillo-Chávez, C., et al. *Epidemiological models with age structure, proportionate mixing, and cross-immunity*. J. Math. Biol., **27** (1989), 233-258.
- [5] Caswell, H. *Matrix Population Models: Construction, Analysis, and Interpretations*. Sinauer, 2001. Ch 9.
- [6] Center for Disease Control (CDC). June 19, 2001. World Wide Web. <http://www.cdc.gov/ncidod/dvbid/dengue/map-distribution-2000.htm>

- [7] Derouich, M., et al. *A Model of Dengue Fever*. Biomedical Engineering Online, (2003). World Wide Web. <http://biomedical.engineering.online.com/content/2/1/4>.
- [8] Esteva, L., Vargas, C. *A model for dengue disease with variable human population*. J. Math. Biol., **38** (1999), pp.220-240.
- [9] Esteva, L., Vargas, C. *Coexistence of different serotypes of dengue virus*. September, 2002. J. Math. Biol. **46**, pp. 31-47.
- [10] Esteva Peralta, Ma. de Lourdes. *Modelos Matemáticos de la Enfermedad del Dengue*. September, 1996. Ph.D. Thesis
- [11] Feng, Z. and Velasco-Hernández, J. *Competitive exclusion in a vector-host model for the dengue fever* J. Math. Biol., **35** (1997), 523-544.
- [12] Gubler, D.J. and Kuno, G. *Dengue and Dengue Hemorrhagic Fever*, CABI Publishing, (1997).
- [13] Harrington, L., et al. *Why Do Female Aedes aegypti (Diptera: Culicidae) Feed Preferentially and Frequently on Human Blood?* J. Medical Entomology, **38** May, 2001.
- [14] Harrington, L., Buonaccorsi, J., Edman, J., Costero, A., Kittayapong, P., Gary Clark, G., and Scott, T., *Analysis of Survival of Young and Old Aedes aegypti (Diptera: Culicidae) from Puerto Rico and Thailand*, J. Med. Entomol., **38**(4) (2001), 537-547
- [15] Kammo, M. and Sasaki, A. *The effect of cross-immunity and seasonal forcing in a multi-strain epidemic model*. Physica D. **165** (2002) 228-241.
- [16] Keating, Joseph, *An investigation into the cyclical incidence of dengue fever*, Social Science & Medicine, **53** (2001), 1587-1597.
- [17] Kokko, H. and Lindström, J. *Seasonal density dependence, timing of mortality, and sustainable harvesting*. Ecological Modelling **110** (1998) 293-304.
- [18] Kurane, I. and Takasaki, T., *Dengue fever and dengue hemorrhagic fever: challenges of controlling an enemy still at large*, Med. Virol., **11** (2001), pp. 301-311.
- [19] Sánchez, F., Engman, M., Castillo-Chávez, C. *Stability of Disease Free and Endemic Equilibria for Models of Dengue Fever*. In revision.
- [20] World Health Organization (WHO). *Communicable Disease Surveillance & Response (CSR)*. 2003. World Wide Web. <http://rhone.b3e.jussieu.fr/DengueNet/>